

APPENDIX A

SEQUENCE LISTING

<110> Dr. Voelkel, Helge

<120> Method for screening of modulators of calcineurin
activity

<130> A34157PCT

<140> PCT/EP99/05220

<141> 1999-07-22

<150> EP98113876

<151> 1998-07-22

<160> 35

<170> PatentIn Ver. 2.1

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35 40 45

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Phe Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg

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His Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala

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Asp Val Ser Ile Glu Asp Ser Val Ile Ser Leu Ser Gly Asp His Cys

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Ile Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly

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35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60

Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80

Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
 85 90 95

Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
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Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
 115 120 125

Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
 130 135 140

Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160

Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
 165 170 175

Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
 180 185 190

Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu
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Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe
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Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys
225 230 235

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<213> Homo sapiens

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Ala Val Pro Phe Pro Pro Thr His Arg Leu Thr Ser Glu Glu Val Phe
35 40 45

Asp Leu Asp Gly Ile Pro Arg Val Asp Val Leu Lys Asn His Leu Val
50 55 60

Lys Glu Gly Arg Val Asp Glu Glu Ile Ala Leu Arg Ile Ile Asn Glu
65 70 75 80

Gly Ala Ala Ile Leu Arg Arg Glu Lys Thr Met Ile Glu Val Glu Ala
85 90 95

Pro Ile Thr Val Cys Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met
100 105 110

Lys Leu Phe Glu Val Gly Gly Ser Pro Ala Asn Thr Arg Tyr Leu Phe
115 120 125

Leu Gly Asp Tyr Val Asp Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu
130 135 140

Tyr Leu Trp Val Leu Lys Ile Leu Tyr Pro Ser Thr Leu Phe Leu Leu
145 150 155 160

Arg Gly Asn His Glu Cys Arg His Leu Thr Glu Tyr Phe Thr Phe Lys
165 170 175

Gln Glu Cys Lys Ile Lys Tyr Ser Glu Arg Val Tyr Glu Ala Cys Met
180 185 190

Glu Ala Phe Asp Ser Leu Pro Leu Ala Ala Leu Leu Asn Gln Gln Phe
195 200 205

Leu Cys Val His Gly Gly Leu Ser Pro Glu Ile His Thr Leu Asp Asp
210 215 220

Ile Arg Arg Leu Asp Arg Phe Lys Glu Pro Pro Ala Phe Gly Pro Met
225 230 235 240

Cys Asp Leu Leu Trp Ser Asp Pro Ser Glu Asp Phe Gly Asn Glu Lys

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Tyr Asn Tyr Pro Ala Val Cys Glu Phe Leu Gln Asn Asn Asn Leu Leu		
275	280	285
Ser Ile Ile Arg Ala His Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr		
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Arg Lys Ser Gln Thr Thr Gly Phe Pro Ser Leu Ile Thr Ile Phe Ser		
305	310	315
Ala Pro Asn Tyr Leu Asp Val Tyr Asn Asn Lys Ala Ala Val Leu Lys		
325	330	335
Tyr Glu Asn Asn Val Met Asn Ile Arg Gln Phe Asn Cys Ser Pro His		
340	345	350
Pro Tyr Trp Leu Pro Asn Phe Met Asp Val Phe Thr Trp Ser Leu Pro		
355	360	365
Phe Val Gly Glu Lys Val Thr Glu Met Leu Val Asn Val Leu Ser Ile		
370	375	380
Cys Ser Asp Asp Glu Leu Met Thr Glu Gly Glu Asp Gln Phe Asp Gly		
385	390	395
Ser Ala Ala Ala Arg Lys Glu Ile Ile Arg Asn Lys Ile Arg Ala Ile		
405	410	415
Gly Lys Met Ala Arg Val Phe Ser Val Leu Arg Glu Glu Ser Glu Ser		
420	425	430
Val Leu Thr Leu Lys Gly Leu Thr Pro Thr Gly Met Leu Pro Ser Gly		
435	440	445
Val Leu Ala Gly Gly Arg Gln Thr Leu Gln Ser Ala Thr Val Glu Ala		
450	455	460
Ile Glu Ala Glu Lys Ala Ile Arg Gly Phe Ser Pro Pro His Arg Ile		
465	470	475
		480

Cys Ser Phe Glu Glu Ala Lys Gly Leu Asp Arg Ile Asn Glu Arg Met
485 490 495

Pro Pro Arg Lys Asp Ala Val Gln Gln Asp Gly Phe Asn Ser Leu Asn
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Thr Ala His Ala Thr Glu Asn His Gly Thr Gly Asn His Thr Ala Gln
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acggtgggag gtctatataa gcagagctgg ttagtgaac cgtcagatcc gctagcgcta 600

ccggtcgcca cc atg gtg agc aag ggc gag gag ctg ttc acc ggg gtg gtg 651

Met Val Ser Lys Gly Glu Glu Leu Phe Thr Gly Val Val

1 5 10

ccc atc ctg gtc gag ctg gac ggc gac gta aac ggc cac aag ttc agc 699

Pro Ile Leu Val Glu Leu Asp Gly Asp Val Asn Gly His Lys Phe Ser

15 20 25

gtg tcc ggc gag ggc gag ggc gat gcc acc tac ggc aag ctg acc ctg 747

Val Ser Gly Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu

30 35 40 45

aag ttc atc tgc acc acc ggc aag ctg ccc gtg ccc tgg ccc acc ctc 795

Lys Phe Ile Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu

50 55 60

gtg acc acc ctg acc tac ggc gtg cag tgc ttc agc cgc tac ccc gac 843

Val Thr Thr Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp

65 70 75

cac atg aag cag cac gac ttc ttc aag tcc gcc atg ccc gaa ggc tac 891

His Met Lys Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr

80 85 90

gtc cag gag cgc acc atc ttc ttc aag gac gac ggc aac tac aag acc 939

Val Gln Glu Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr

95 100 105

cgc gcc gag gtg aag ttc gag ggc gac acc ctg gtg aac cgc atc gag 987

Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu

110 115 120 125

ctg aag ggc atc gac ttc aag gag gac ggc aac atc ctg ggg cac aag 1035

Leu Lys Gly Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys

130 135 140

ctg gag tac aac tac aac agc cac aac gtc tat atc atg gcc gac aag 1083

Leu Glu Tyr Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys

145 150 155

cag aag aac ggc atc aag gtg aac ttc aag atc cgc cac aac atc gag 1131
 Gln Lys Asn Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu
 160 165 170

gac ggc agc gtg cag ctc gcc gac cac tac cag cag aac acc ccc atc 1179
 Asp Gly Ser Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile
 175 180 185

ggc gac ggc ccc gtg ctg ctg ccc gac aac cac tac ctg agc acc cag 1227
 Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln
 190 195 200 205

tcc gcc ctg agc aaa gac ccc aac gag aag cgc gat cac atg gtc ctg 1275
 Ser Ala Leu Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu
 210 215 220

ctg gag ttc gtg acc gcc gcc ggg atc act ctc ggc atg gac gag ctg 1323
 Leu Glu Phe Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu
 225 230 235

tac aag tcc gga ctc aga tcc aga tcc atg tcc ggg agg cgc ttc cac 1371
 Tyr Lys Ser Gly Leu Arg Ser Arg Ser Met Ser Gly Arg Arg Phe His
 240 245 250

ctc tcc acc acc gac cgc gtc atc aaa gct gtc ccc ttt cct cca acc 1419
 Leu Ser Thr Thr Asp Arg Val Ile Lys Ala Val Pro Phe Pro Pro Thr
 255 260 265

caa cgg ctt act ttc aag gaa gta ttt gag aat ggg aaa cct aaa gtt 1467
 Gln Arg Leu Thr Phe Lys Glu Val Phe Glu Asn Gly Lys Pro Lys Val
 270 275 280 285

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 Asp Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu Glu Glu Glu
 290 295 300

gta gcc tta aag ata atc aat gat ggg gct gcc atc ctg agg caa gag 1563
 Val Ala Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu Arg Gln Glu
 305 310 315

aag act atg ata gaa gta gat gct cca atc aca gta tgt ggt gat att 1611
 Lys Thr Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys Gly Asp Ile
 320 325 330

cat gga caa ttc ttt gac cta atg aag tta ttt gaa gtt gga gga tca 1659
 His Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser
 335 340 345

cct agt aac aca cgc tac ctc ttt ctg ggt gac tat gtg gac aga ggc 1707
 Pro Ser Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly
 350 355 360 365

tat ttc agt ata gag tgt gtg ctg tat tta tgg agt tta aag att aat 1755
 Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu Lys Ile Asn
 370 375 380

cat ccc aaa aca ttg ttt ctg ctt cgg gga aat cat gaa tgc agg cat 1803
 His Pro Lys Thr Leu Phe Phe Leu Arg Gly Asn His Glu Cys Arg His
 385 390 395

ctt aca gac tat ttc acc ttc aaa cag gaa tgt cga atc aaa tat tcg 1851
 Leu Thr Asp Tyr Phe Thr Phe Lys Gln Glu Cys Arg Ile Lys Tyr Ser
 400 405 410

gaa cag gtg tat gat gcc tgt atg gag aca ttt gac tgt ctt cct ctt 1899
 Glu Gln Val Tyr Asp Ala Cys Met Glu Thr Phe Asp Cys Leu Pro Leu
 415 420 425

gct gcc ctc tta aac cag cag ttt ctc tgt gta cat gga gga atg tca 1947
 Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly Met Ser
 430 435 440 445

cct gaa att act tct tta gat gac att agg aaa tta gac agg ttt acg 1995
 Pro Glu Ile Thr Ser Leu Asp Asp Ile Arg Lys Leu Asp Arg Phe Thr
 450 455 460

gaa cct ccc gcc ttt gga cct gtg tgt gac ctg ctt tgg tct gat ccc 2043
 Glu Pro Pro Ala Phe Gly Pro Val Cys Asp Leu Leu Trp Ser Asp Pro
 465 470 475

tca gag gat tat ggc aat gag aag acc ttg gag cac tat acc cac aac 2091
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 480 485 490

act gtc cga ggg tgc tct tat ttc tac agt tac cct gca gtt tgt gaa 2139
 Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala Val Cys Glu
 495 500 505

ttt ttg cag aac aat aat tta cta tca att atc aga gcc cat gaa gcc 2187
Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His Glu Ala
510 515 520 525

caa gat gct ggg tat cga atg tac agg aag agc caa gcc aca ggc ttt 2235
Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Ala Thr Gly Phe
530 535 540

cca tca ctt att aca att ttc tct gcc ccc aat tac cta gat gtc tat 2283
Pro Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu Asp Val Tyr
545 550 555

aac aat aaa gct gct gtg ttg aaa tat gaa aac aat gtc atg aat atc 2331
Asn Asn Lys Ala Ala Val Leu Lys Tyr Glu Asn Asn Val Met Asn Ile
560 565 570

agg cag ttt aac tgt tct cca cac ccc tac tgg ctt cca aac ttt atg 2379
Arg Gln Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro Asn Phe Met
575 580 585

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Asp Val Phe Thr Trp Ser Leu Pro Phe Val Gly Glu Lys Val Thr Glu
590 595 600 605

atg ctg gta aat gtg ctc aac ata tgc tct gat gac gaa ctg att tct 2475
Met Leu Val Asn Val Leu Asn Ile Cys Ser Asp Asp Glu Leu Ile Ser
610 615 620

gat gat gaa gca gaa gga agc act aca gtt cgt aag gag atc atc agg 2523
Asp Asp Glu Ala Glu Gly Ser Thr Thr Val Arg Lys Glu Ile Ile Arg
625 630 635

aat aag atc aga gcc att ggg aag atg gca cgg gtc ttt tca att ctt 2571
Asn Lys Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe Ser Ile Leu
640 645 650

cgg caa gaa agt gag agt gtg ctg act ctc aag ggc ctg act ccc aca 2619
Arg Gln Glu Ser Glu Ser Val Leu Thr Leu Lys Gly Leu Thr Pro Thr
655 660 665

ggc aca ctc cct ctg ggc gtc ctc tca gga ggc aag cag act atc gag 2667
Gly Thr Leu Pro Leu Gly Val Leu Ser Gly Gly Lys Gln Thr Ile Glu
670 675 680 685

aca gcc atc aga ggg ttc tcg ctt cag cac aag atc cgg agt ttt gaa 2715
 Thr Ala Ile Arg Gly Phe Ser Leu Gln His Lys Ile Arg Ser Phe Glu
 690 695 700

gaa gcg cga ggt ctg gac cga att aat gag cga atg cca ccc cga aag 2763
 Glu Ala Arg Gly Leu Asp Arg Ile Asn Glu Arg Met Pro Pro Arg Lys
 705 710 715

gat agc ata tac cct ggt ggg cca atg aaa tct gta acc tca gca cac 2811
 Asp Ser Ile Tyr Pro Gly Gly Pro Met Lys Ser Val Thr Ser Ala His
 720 725 730

tca cat gct gcg cac agg agc gac caa ggg aag aaa gcc cat tca 2856
 Ser His Ala Ala His Arg Ser Asp Gln Gly Lys Lys Ala His Ser
 735 740 745

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at

6218

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Glu Gly Glu Gly Asp Ala Thr Tyr Gly Lys Leu Thr Leu Lys Phe Ile
35 40 45
Cys Thr Thr Gly Lys Leu Pro Val Pro Trp Pro Thr Leu Val Thr Thr
50 55 60
Leu Thr Tyr Gly Val Gln Cys Phe Ser Arg Tyr Pro Asp His Met Lys
65 70 75 80
Gln His Asp Phe Phe Lys Ser Ala Met Pro Glu Gly Tyr Val Gln Glu
85 90 95
Arg Thr Ile Phe Phe Lys Asp Asp Gly Asn Tyr Lys Thr Arg Ala Glu
100 105 110
Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu Leu Lys Gly
115 120 125
Ile Asp Phe Lys Glu Asp Gly Asn Ile Leu Gly His Lys Leu Glu Tyr
130 135 140
Asn Tyr Asn Ser His Asn Val Tyr Ile Met Ala Asp Lys Gln Lys Asn
145 150 155 160
Gly Ile Lys Val Asn Phe Lys Ile Arg His Asn Ile Glu Asp Gly Ser
165 170 175
Val Gln Leu Ala Asp His Tyr Gln Gln Asn Thr Pro Ile Gly Asp Gly
180 185 190
Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln Ser Ala Leu

195

200

205

Ser Lys Asp Pro Asn Glu Lys Arg Asp His Met Val Leu Leu Glu Phe

210

215

220

Val Thr Ala Ala Gly Ile Thr Leu Gly Met Asp Glu Leu Tyr Lys

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<211> 509

<212> PRT

<213> Homo sapiens

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Leu Thr Phe Lys Glu Val Phe Glu Asn Gly Lys Pro Lys Val Asp Val

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Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu Glu Glu Glu Val Ala

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55

60

Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu Arg Gln Glu Lys Thr

65

70

75

80

Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys Gly Asp Ile His Gly

85

90

95

Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro Ser

100

105

110

Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr Phe

115

120

125

Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu Lys Ile Asn His Pro

130

135

140

Lys Thr Leu Phe Leu Leu Arg Gly Asn His Glu Cys Arg His Leu Thr

145 150 155 160
 Asp Tyr Phe Thr Phe Lys Gln Glu Cys Arg Ile Lys Tyr Ser Glu Gln
 165 170 175
 Val Tyr Asp Ala Cys Met Glu Thr Phe Asp Cys Leu Pro Leu Ala Ala
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 Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly Met Ser Pro Glu
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 Ile Thr Ser Leu Asp Asp Ile Arg Lys Leu Asp Arg Phe Thr Glu Pro
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 Pro Ala Phe Gly Pro Val Cys Asp Leu Leu Trp Ser Asp Pro Ser Glu
 225 230 235 240
 Asp Tyr Gly Asn Glu Lys Thr Leu Glu His Tyr Thr His Asn Thr Val
 245 250 255
 Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala Val Cys Glu Phe Leu
 260 265 270
 Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His Glu Ala Gln Asp
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 Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Ala Thr Gly Phe Pro Ser
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 Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu Asp Val Tyr Asn Asn
 305 310 315 320
 Lys Ala Ala Val Leu Lys Tyr Glu Asn Asn Val Met Asn Ile Arg Gln
 325 330 335
 Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro Asn Phe Met Asp Val
 340 345 350
 Phe Thr Trp Ser Leu Pro Phe Val Gly Glu Lys Val Thr Glu Met Leu
 355 360 365
 Val Asn Val Leu Asn Ile Cys Ser Asp Asp Glu Leu Ile Ser Asp Asp
 370 375 380

Glu Ala Glu Gly Ser Thr Thr Val Arg Lys Glu Ile Ile Arg Asn Lys
385 390 395 400

Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe Ser Ile Leu Arg Gln
 405 410 415

Glu Ser Glu Ser Val Leu Thr Leu Lys Gly Leu Thr Pro Thr Gly Thr
 420 425 430

Leu Pro Leu Gly Val Leu Ser Gly Gly Lys Gln Thr Ile Glu Thr Ala
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Ile Arg Gly Phe Ser Leu Gln His Lys Ile Arg Ser Phe Glu Glu Ala
 450 455 460

Arg Gly Leu Asp Arg Ile Asn Glu Arg Met Pro Pro Arg Lys Asp Ser
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ggatcgcatc accatcacca tcacggatcc gcg acg aag gcc gtg tgc gtg ctg 174

Ala Thr Lys Ala Val Cys Val Leu

1 5

aag ggc gac ggc cca gtg cag ggc atc atc aat ttc gag cag aag gaa 222

Lys Gly Asp Gly Pro Val Gln Gly Ile Ile Asn Phe Glu Gln Lys Glu

10 15 20

agt aat gga cca gtg aag gtg tgg gga agc att aaa gga ctg act gaa 270

Ser Asn Gly Pro Val Lys Val Trp Gly Ser Ile Lys Gly Leu Thr Glu

25 30 35 40

ggc ctg cat gga ttc cat gtt cat gag ttt gga gat aat aca gca ggc 318

Gly Leu His Gly Phe His Val His Glu Phe Gly Asp Asn Thr Ala Gly

45 50 55

tgt acc agt gca ggt cct cac ttt aat cct cta tcc aga aaa cac ggt 366

Cys Thr Ser Ala Gly Pro His Phe Asn Pro Leu Ser Arg Lys His Gly

60 65 70

ggg cca aag gat gaa gag agg cat gtt gga gac ttg ggc aat gtg act 414

Gly Pro Lys Asp Gly Glu Arg His Val Gly Asp Leu Gly Asn Val Thr

75 80 85

gct gac aaa gat ggt gtg gcc gat gtg tct att gaa gat tct gtg atc 462

Ala Asp Lys Asp Gly Val Ala Asp Val Ser Ile Glu Asp Ser Val Ile

90 95 100

tca ctc tca gga gac cat tgc atc att ggc cgc aca ctg gtg gtc cat 510

Ser Leu Ser Gly Asp His Cys Ile Ile Gly Arg Thr Leu Val Val His

105 110 115 120

gaa aaa gca gat gac ttg ggc aaa ggt gga aat gaa gaa agt aca aag 558

Glu Lys Ala Asp Asp Leu Gly Lys Gly Asn Glu Glu Ser Thr Lys

125 130 135

aca gga aac gct gga agt cgt ttg gct tgt ggt gta att ggg atc gcc 606
 Thr Gly Asn Ala Gly Ser Arg Leu Ala Cys Gly Val Ile Gly Ile Ala
 140 145 150

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3975

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<213> Homo sapiens

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10

15

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 Gly Ser Ile Lys Gly Leu Thr Glu Gly Leu His Gly Phe His Val His
 35 40 45
 Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His Phe
 50 55 60
 Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg His
 65 70 75 80
 Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala Asp
 85 90 95
 Val Ser Ile Glu Asp Ser Val Ile Ser Leu Ser Gly Asp His Cys Ile
 100 105 110
 Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly Lys
 115 120 125
 Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser Arg Leu
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 145 150

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 <223> carboxypeptidase-A cleavage site

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<222> (578)..(603)

<223> histidine tag

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Met

1

gcg acg aag gcc gtg tgc gtg ctg aag ggc gac ggc cca gtg cag ggc 165

Ala Thr Lys Ala Val Cys Val Leu Lys Gly Asp Gly Pro Val Gln Gly

5 10 15

atc atc aat ttc gag cag aag gaa agt aat gga cca gtg aag gtg tgg 213

Ile Ile Asn Phe Glu Gln Lys Glu Ser Asn Gly Pro Val Lys Val Trp

20 25 30

gga agc att aaa gga ctg act gaa ggc ctg cat gga ttc cat gtt cat 261

Gly Ser Ile Lys Gly Leu Thr Glu Gly Leu His Gly Phe His Val His

35 40 45

gag ttt gga gat aat aca gca ggc tgt acc agt gca ggt cct cac ttt 309

Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His Phe

50 55 60 65

aat cct cta tcc aga aaa cac ggt ggg cca aag gat gaa gag agg cat 357

Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg His

70 75 80

gtt gga gac ttg ggc aat gtg act gct gac aaa gat ggt gtg gcc gat 405

Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala Asp

85 90 95

gtg tct att gaa gat tct gtg atc tca ctc tca gga gac cat tgc atc 453

Val Ser Ile Glu Asp Ser Val Ile Ser Leu Ser Gly Asp His Cys Ile

100 105 110

att ggc cgc aca ctg gtg gtc cat gaa aaa gca gat gac ttg ggc aaa 501

Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly Lys

115 120 125

ggt gga aat gaa gaa agt aca aag aca gga aac gct gga agt cgt ttg 549
 Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser Arg Leu
 130 135 140 145

gct tgt ggt gta att ggg atc gcc caa agatctcatc accatcacca 596
 Ala Cys Gly Val Ile Gly Ile Ala Gln
 150

tcactaagct taattagctg agcttggact cctgttgata gatccagtaa tgacctcaga 656
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Trp Gly Ser Ile Lys Gly Leu Thr Glu Gly Leu His Gly Phe His Val
35 40 45

His Glu Phe Gly Asp Asn Thr Ala Gly Cys Thr Ser Ala Gly Pro His
50 55 60

Phe Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu Arg
65 70 75 80

His Val Gly Asp Leu Gly Asn Val Thr Ala Asp Lys Asp Gly Val Ala
85 90 95

Asp Val Ser Ile Glu Asp Ser Val Ile Ser Leu Ser Gly Asp His Cys
100 105 110

Ile Ile Gly Arg Thr Leu Val Val His Glu Lys Ala Asp Asp Leu Gly
115 120 125

Lys Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser Arg
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Leu Ala Cys Gly Val Ile Gly Ile Ala Gln
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<223> histidine tagged calcineurin A alpha1

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<222> (1714)..(1758)
<223> ribosomal binding site, multiple cloning site 2

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<221> CDS

<222> (1759)..(2268)

<223> calcineurin B

<220>

<221> variation

<222> (115)..(1713)

<223> splicevariant: histidine tagged calcineurin A

alpha1 lacking pos. 208 - 2317 (phosphatase

domain), newly generated N-terminus exhibits

protease activity

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attgtgagcg gataacaatt tcacacagaa ttcattaaag aggagaaatt aactatg 117

Met

1

aga gga tcg cat cac cat cac cat cac gga tcc atg tcc gag ccc aag 165

Arg Gly Ser His His His His His His Gly Ser Met Ser Glu Pro Lys

5 10 15

gca att gat ccc aag ttg tcg acg acc gac agg gtg gtg aaa gct gtt 213

Ala Ile Asp Pro Lys Leu Ser Thr Thr Asp Arg Val Val Lys Ala Val

20 25 30

cca ttt cct cca agt cac cgg ctt aca gca aaa gaa gtg ttt gat aat 261

Pro Phe Pro Pro Ser His Arg Leu Thr Ala Lys Glu Val Phe Asp Asn

35 40 45

gat gga aaa cct cgt gtg gat atc tta aag gcg cat ctt atg aag gag 309

Asp Gly Lys Pro Arg Val Asp Ile Leu Lys Ala His Leu Met Lys Glu

50 55 60 65

gga agg ctg gaa gag agt gtt gca ttg aga ata ata aca gag ggt gca 357

Gly Arg Leu Glu Glu Ser Val Ala Leu Arg Ile Ile Thr Glu Gly Ala

70 75 80

tca att ctt cga cag gaa aaa aat ttg ctg gat att gat gcg cca gtc 405

Ser Ile Leu Arg Gln Glu Lys Asn Leu Leu Asp Ile Asp Ala Pro Val

85 90 95

act gtt tgt ggg gac att cat gga caa ttc ttt gat ttg atg aag ctc 453

Thr Val Cys Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys Leu
100 105 110

ttt gaa gtc ggg gga tct cct gcc aac act cgc tac ctc ttc tta ggg 501
Phe Glu Val Gly Gly Ser Pro Ala Asn Thr Arg Tyr Leu Phe Leu Gly
115 120 125

gac tat gtt gac aga ggg tac ttc agt att gaa tgt gtg ctg tat ttg 549
Asp Tyr Val Asp Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu
130 135 140 145

tgg gcc ttg aaa att ctc tac ccc aaa aca ctg ttt tta ctt cgt gga 597
Trp Ala Leu Lys Ile Leu Tyr Pro Lys Thr Leu Phe Leu Leu Arg Gly
150 155 160

aat cat gaa tgt aga cat cta aca gag tat ttc aca ttt aaa caa gaa 645
Asn His Glu Cys Arg His Leu Thr Glu Tyr Phe Thr Phe Lys Gln Glu
165 170 175

tgt aaa ata aag tat tca gaa cga gta tat gat gcc tgt atg gat gcc 693
Cys Lys Ile Lys Tyr Ser Glu Arg Val Tyr Asp Ala Cys Met Asp Ala
180 185 190

ttt gac tgc ctt ccc ctg gct gcc ctg atg aac caa cag ttc ctg tgt 741
Phe Asp Cys Leu Pro Leu Ala Ala Leu Met Asn Gln Gln Phe Leu Cys
195 200 205

gtg cat ggt ggt ttg tct cca gag att aac act tta gat gat atc aga 789
Val His Gly Gly Leu Ser Pro Glu Ile Asn Thr Leu Asp Asp Ile Arg
210 215 220 225

aaa tta gac cga ttc aaa gaa cca cct gca tat gga cct atg tgt gat 837
Lys Leu Asp Arg Phe Lys Glu Pro Pro Ala Tyr Gly Pro Met Cys Asp
230 235 240

atc ctg tgg tca gac ccc ctg gaa gat ttt gga aat gag aag act cag 885
Ile Leu Trp Ser Asp Pro Leu Glu Asp Phe Gly Asn Glu Lys Thr Gln
245 250 255

gaa cat ttc act cac aac aca gtc agg ggg tgt tca tac ttc tac agt 933
Glu His Phe Thr His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser
260 265 270

tac ccg gct gta tgt gaa ttc tta cag cac aat aac ttg tta tct ata 981
Tyr Pro Ala Val Cys Glu Phe Leu Gln His Asn Asn Leu Leu Ser Ile
275 280 285

ctc cga gcc cac gaa gcc caa gat gca ggg tac cgc atg tac agg aaa 1029
Leu Arg Ala His Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys
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Asn Tyr Leu Asp Val Tyr Asn Asn Lys Ala Ala Val Leu Lys Tyr Glu
325 330 335

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Asn Asn Val Met Asn Ile Arg Gln Phe Asn Cys Ser Pro His Pro Tyr
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Trp Leu Pro Asn Phe Met Asp Val Phe Thr Trp Ser Leu Pro Phe Val
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370 375 380 385

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Asp Asp Glu Leu Gly Ser Glu Glu Asp Gly Phe Asp Gly Ala Thr Ala
390 395 400

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Thr Leu Lys Gly Leu Thr Pro Thr Gly Met Leu Pro Ser Gly Val Leu
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 Ser Asn Ile Gln
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Leu Asp Ile His Lys Lys Met Val Val Asp Val
695 700 705

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35 40 45

Asn Asp Gly Lys Pro Arg Val Asp Ile Leu Lys Ala His Leu Met Lys

50 55 60

Glu Gly Arg Leu Glu Glu Ser Val Ala Leu Arg Ile Ile Thr Glu Gly

65 70 75 80

Ala Ser Ile Leu Arg Gln Glu Lys Asn Leu Leu Asp Ile Asp Ala Pro

85 90 95

Val Thr Val Cys Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys

100 105 110

Leu Phe Glu Val Gly Gly Ser Pro Ala Asn Thr Arg Tyr Leu Phe Leu

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Gly Asp Tyr Val Asp Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr

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Leu Trp Ala Leu Lys Ile Leu Tyr Pro Lys Thr Leu Phe Leu Leu Arg

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Gly Asn His Glu Cys Arg His Leu Thr Glu Tyr Phe Thr Phe Lys Gln

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Glu Cys Lys Ile Lys Tyr Ser Glu Arg Val Tyr Asp Ala Cys Met Asp

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Cys Val His Gly Gly Leu Ser Pro Glu Ile Asn Thr Leu Asp Asp Ile		
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Asp Ile Leu Trp Ser Asp Pro Leu Glu Asp Phe Gly Asn Glu Lys Thr		
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Gln Glu His Phe Thr His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr		
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Ser Tyr Pro Ala Val Cys Glu Phe Leu Gln His Asn Asn Leu Leu Ser		
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Ile Leu Arg Ala His Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg		
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Lys Ser Gln Thr Thr Gly Phe Pro Ser Leu Ile Thr Ile Phe Ser Ala		
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Pro Asn Tyr Leu Asp Val Tyr Asn Asn Lys Ala Ala Val Leu Lys Tyr		
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Glu Asn Asn Val Met Asn Ile Arg Gln Phe Asn Cys Ser Pro His Pro		
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Tyr Trp Leu Pro Asn Phe Met Asp Val Phe Thr Trp Ser Leu Pro Phe		
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Val Gly Glu Lys Val Thr Glu Met Leu Val Asn Val Leu Asn Ile Cys		
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Ser Asp Asp Glu Leu Gly Ser Glu Glu Asp Gly Phe Asp Gly Ala Thr		
385	390	395 400
Ala Ala Ala Arg Lys Glu Val Ile Arg Asn Lys Ile Arg Ala Ile Gly		
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Lys Met Ala Arg Val Phe Ser Val Leu Arg Glu Glu Ser Glu Ser Val
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Leu Thr Leu Lys Gly Leu Thr Pro Thr Gly Met Leu Pro Ser Gly Val
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Ser Phe Glu Glu Ala Lys Gly Leu Asp Arg Ile Asn Glu Arg Met Pro
485 490 495

Pro Arg Arg Asp Ala Met Pro Ser Asp Ala Asn Leu Asn Ser Ile Asn
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35 40 45

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Gln Phe Ser Val Lys Gly Asp Lys Glu Gln Lys Leu Arg Phe Ala Phe
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Arg Ile Tyr Asp Met Asp Lys Asp Gly Tyr Ile Ser Asn Gly Glu Leu
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Phe Gln Val Leu Lys Met Met Val Gly Asn Asn Leu Lys Asp Thr Gln
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Leu Gln Gln Ile Val Asp Lys Thr Ile Ile Asn Ala Asp Lys Asp Gly
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Arg Gly Ser His His His His His Gly Ser Met Ser Glu Pro Lys

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Ala Ile Asp Pro Lys Leu Ser Thr Thr Asp Arg Val Val Lys Ala Val

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cca ttt cct cca agt cac cgg ctt aca gca aaa gaa gtg ttt gat aat 261

Pro Phe Pro Pro Ser His Arg Leu Thr Ala Lys Glu Val Phe Asp Asn

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gat gga aaa cct cgt gtg gat atc tta aag gcg cat ctt atg aag gag 309

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Ser Ile Leu Arg Gln Glu Lys Asn Leu Leu Asp Ile Asp Ala Pro Val

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90

95

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105

110

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130

135

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 230 235 240

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 Glu His Phe Thr His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser
 260 265 270

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 680 685 690

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Val Thr Val Cys Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys
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Ala Phe Asp Cys Leu Pro Leu Ala Ala Leu Met Asn Gln Gln Phe Leu
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Cys Val His Gly Gly Leu Ser Pro Glu Ile Asn Thr Leu Asp Asp Ile
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25

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680 685 690

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 35 40 45
 Leu Thr Ser Glu Glu Val Phe Asp Leu Asp Gly Ile Pro Arg Val Asp
 50 55 60
 Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Val Asp Glu Glu Ile
 65 70 75 80
 Ala Leu Arg Ile Ile Asn Glu Gly Ala Ala Ile Leu Arg Arg Glu Lys
 85 90 95

Thr Met Ile Glu Val Glu Ala Pro Ile Thr Val Cys Gly Asp Ile His
100 105 110

Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro
115 120 125

Ala Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr
130 135 140

Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Val Leu Lys Ile Leu Tyr
145 150 155 160

Pro Ser Thr Leu Phe Leu Leu Arg Gly Asn His Glu Cys Arg His Leu
165 170 175

Thr Glu Tyr Phe Thr Phe Lys Gln Glu Cys Lys Ile Lys Tyr Ser Glu
180 185 190

Arg Val Tyr Glu Ala Cys Met Glu Ala Phe Asp Ser Leu Pro Leu Ala
195 200 205

Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly Leu Ser Pro
210 215 220

Glu Ile His Thr Leu Asp Asp Ile Arg Arg Leu Asp Arg Phe Lys Glu
225 230 235 240

Pro Pro Ala Phe Gly Pro Met Cys Asp Leu Leu Trp Ser Asp Pro Ser
245 250 255

Glu Asp Phe Gly Asn Glu Lys Ser Gln Glu His Phe Ser His Asn Thr
260 265 270

Val Arg Gly Cys Ser Tyr Phe Tyr Asn Tyr Pro Ala Val Cys Glu Phe
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Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His Glu Ala Gln
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Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Thr Thr Gly Phe Pro
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Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu Asp Val Tyr Asn

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 385 390 395 400
 Gly Glu Asp Gln Phe Asp Gly Ser Ala Ala Ala Arg Lys Glu Ile Ile
 405 410 415
 Arg Asn Lys Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe Ser Val
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 Thr Gly Met Leu Pro Ser Gly Val Leu Ala Gly Gly Arg Gln Thr Leu
 450 455 460
 Gln Ser Ala Thr Val Glu Ala Ile Glu Ala Glu Lys Ala Ile Arg Gly
 465 470 475 480
 Phe Ser Pro Pro His Arg Ile Cys Ser Phe Glu Glu Ala Lys Gly Leu
 485 490 495
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35 40 45

Leu Gln Gln Asn Xaa Leu Val Gln Arg Val Ile Asp Ile Phe Asp Thr
50 55 60

Asp Gly Asn Gly Glu Val Asp Phe Lys Glu Phe Ile Glu Xaa Val Ser
65 70 75 80

Gln Phe Ser Val Lys Gly Asp Lys Glu Gln Lys Leu Arg Phe Ala Phe
85 90 95

Arg Ile Tyr Asp Met Asp Lys Asp Gly Tyr Ile Ser Asn Gly Glu Leu
100 105 110

Phe Gln Xaa Xaa Lys Met Met Val Gly Asn Asn Leu Lys Asp Thr Gln
115 120 125

Leu Gln Gln Ile Val Asp Lys Thr Ile Ile Asn Ala Asp Lys Asp Xaa
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165 170

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Arg Gly Ser His His His His His His Gly Ser Ala Ala Pro Glu Pro
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Ala Arg Ala Ala Pro Pro Pro Pro Pro Pro Pro Pro Pro Pro Gly
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gct gac cgc gtc gtc aaa gct gtc cct ttc ccc cca aca cat cgc ttg 261
Ala Asp Arg Val Val Lys Ala Val Pro Phe Pro Pro Thr His Arg Leu
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aca tct gaa gaa gta ttt gat ttg gat ggg ata ccc agg gtt gat gtt 309

Thr Ser Glu Glu Val Phe Asp Leu Asp Gly Ile Pro Arg Val Asp Val
50 55 60 65

ctg aag aac cac ttg gtg aaa gaa ggt cga gta gat gaa gaa att gcg 357
Leu Lys Asn His Leu Val Lys Glu Gly Arg Val Asp Glu Glu Ile Ala
70 75 80

ctt aga att atc aat gag ggt gct gcc atc ctt cgg aga gag aaa acc 405
Leu Arg Ile Ile Asn Glu Gly Ala Ala Ile Leu Arg Arg Glu Lys Thr
85 90 95

atg ata gaa gta gaa gct cca atc aca gtg tgt ggt gac atc cat ggc 453
Met Ile Glu Val Glu Ala Pro Ile Thr Val Cys Gly Asp Ile His Gly
100 105 110

caa ttt ttt gat ctg atg aaa ctt ttt gaa gta gga gga tca cct gct 501
Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro Ala
115 120 125

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Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr Phe
130 135 140 145

agt ata gag cat gtt cta ggc act gaa gac ata tcg att aat cct cac 597
Ser Ile Glu His Val Leu Gly Thr Glu Asp Ile Ser Ile Asn Pro His
150 155 160

aat aat att aat gag tgt gtc tta tat tta tgg gtt ctg aag att cta 645
Asn Asn Ile Asn Glu Cys Val Leu Tyr Leu Trp Val Leu Lys Ile Leu
165 170 175

tac cca agc aca tta ttt ctt ctg aga ggc aac cat gaa tgc aga cac 693
Tyr Pro Ser Thr Leu Phe Leu Leu Arg Gly Asn His Glu Cys Arg His
180 185 190

ctt act gaa tat ttt acc ttt aag cag gaa tgt aaa att aag tat tcg 741
Leu Thr Glu Tyr Phe Thr Phe Lys Gln Glu Cys Lys Ile Lys Tyr Ser
195 200 205

gaa aga gtc tat gaa gct tgt atg gaa gct ttt gat agt ttg cct ctt 789
Glu Arg Val Tyr Glu Ala Cys Met Glu Ala Phe Asp Ser Leu Pro Leu
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 Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly Leu Ser
 230 235 240

cca gaa ata cac aca ctg gat gat att agg aga tta gat aga ttc aaa 885
 Pro Glu Ile His Thr Leu Asp Asp Ile Arg Arg Leu Asp Arg Phe Lys
 245 250 255

gag cca cct gca ttt gga cca atg tgt gac ttg tta tgg tcc gat cct 933
 Glu Pro Pro Ala Phe Gly Pro Met Cys Asp Leu Leu Trp Ser Asp Pro
 260 265 270

tct gaa gat ttt gga aat gaa aaa tca cag gaa cat ttt agt cac aat 981
 Ser Glu Asp Phe Gly Asn Glu Lys Ser Gln Glu His Phe Ser His Asn
 275 280 285

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 Thr Val Arg Gly Cys Ser Tyr Phe Tyr Asn Tyr Pro Ala Val Cys Glu
 290 295 300 305

ttt ttg caa aac aat aat ttg tta tcg att att aga gct cat gaa gct 1077
 Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His Glu Ala
 310 315 320

caa gat gca ggc tat aga atg tac aga aaa agt caa act aca ggg ttc 1125
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 325 330 335

cct tca tta ata aca att ttt tcg gca cct aat tac tta gat gtc tac 1173
 Pro Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu Asp Val Tyr
 340 345 350

aat aat aaa gct gct gta tta aag tat gaa aat aat gtg atg aat att 1221
 Asn Asn Lys Ala Ala Val Leu Lys Tyr Glu Asn Asn Val Met Asn Ile
 355 360 365

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 Asp Val Phe Thr Trp Ser Leu Pro Phe Val Gly Glu Lys Val Thr Glu
 390 395 400

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 Ile Arg Asn Lys Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe Ser
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 450 455 460 465

ccc aca ggg atg ttg cct agt gga gtg tta gct gga gga cgg cag acc 1557
 Pro Thr Gly Met Leu Pro Ser Gly Val Leu Ala Gly Gly Arg Gln Thr
 470 475 480

ctg caa agt gcc aca gtt gag gct att gag gct gaa aaa gca ata cga 1605
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 485 490 495

gga ttc tct cca cca cat aga atc tgc agt ttt gaa gag gca aag ggt 1653
 Gly Phe Ser Pro His Arg Ile Cys Ser Phe Glu Glu Ala Lys Gly
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 515 520 525

caa gat ggt ttc aat tct ctg aac acc gca cat gcc act gag aac cac 1749
 Gln Asp Gly Phe Asn Ser Leu Asn Thr Ala His Ala Thr Glu Asn His
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Cys Ser His Phe Asp Xaa Asp Glu Ile Lys Arg Leu Gly Lys Arg Phe
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585 590 595

atg tct ctr cct gag tta caa cag aat ccy tta gta cag cga gta ata 1991
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600 605 610

gat ata ttc gac aca gat ggg aat gga gaa gta gac ttt aaa gar ttc 2039
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615 620 625

att gag ggm gtc tct cag ttc agt gtc aaa gga gat aag gar cag aar 2087
Ile Glu Xaa Val Ser Gln Phe Ser Val Lys Gly Asp Lys Glu Gln Lys
630 635 640 645

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650 655 660

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665 670 675

ctg aaa gat aca cag tta cag caa att gta gac aaa acc ata ata aat 2231
Leu Lys Asp Thr Gln Leu Gln Gln Ile Val Asp Lys Thr Ile Ile Asn
680 685 690

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Ala Asp Lys Asp Xaa Asp Gly Arg Ile Ser Phe Glu Glu Phe Cys Ala
695 700 705

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Val Val Xaa Gly Leu Asp Ile His Lys Lys Met Val Val Asp Val
710 715 720 725

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Thr Met Ile Glu Val Glu Ala Pro Ile Thr Val Cys Gly Asp Ile His
100 105 110

Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly Gly Ser Pro
115 120 125

Ala Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp Arg Gly Tyr
130 135 140

Phe Ser Ile Glu His Val Leu Gly Thr Glu Asp Ile Ser Ile Asn Pro
145 150 155 160

His Asn Asn Ile Asn Glu Cys Val Leu Tyr Leu Trp Val Leu Lys Ile
165 170 175

Leu Tyr Pro Ser Thr Leu Phe Leu Leu Arg Gly Asn His Glu Cys Arg
180 185 190

His Leu Thr Glu Tyr Phe Thr Phe Lys Gln Glu Cys Lys Ile Lys Tyr
195 200 205

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210 215 220

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Ser Pro Glu Ile His Thr Leu Asp Asp Ile Arg Arg Leu Asp Arg Phe
245 250 255

Lys Glu Pro Pro Ala Phe Gly Pro Met Cys Asp Leu Leu Trp Ser Asp
260 265 270

Pro Ser Glu Asp Phe Gly Asn Glu Lys Ser Gln Glu His Phe Ser His
275 280 285

Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Asn Tyr Pro Ala Val Cys
290 295 300

Glu Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His Glu
305 310 315 320

Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Thr Thr Gly

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Tyr Asn Asn Lys Ala Ala Val Leu Lys Tyr Glu Asn Asn Val Met Asn		
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Ile Arg Gln Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro Asn Phe		
370	375	380
Met Asp Val Phe Thr Trp Ser Leu Pro Phe Val Gly Glu Lys Val Thr		
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Glu Met Leu Val Asn Val Leu Ser Ile Cys Ser Asp Asp Glu Leu Met		
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Thr Glu Gly Glu Asp Gln Phe Asp Gly Ser Ala Ala Ala Arg Lys Glu		
420	425	430
Ile Ile Arg Asn Lys Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe		
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Ser Val Leu Arg Glu Glu Ser Glu Ser Val Leu Thr Leu Lys Gly Leu		
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465	470	475 480
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Arg Gly Phe Ser Pro Pro His Arg Ile Cys Ser Phe Glu Glu Ala Lys		
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Gly Leu Asp Arg Ile Asn Glu Arg Met Pro Pro Arg Lys Asp Ala Val		
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Xaa Asp Glu Ile Lys Arg Leu Gly Lys Arg Phe Lys Lys Xaa Asp Leu

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Asp Asn Ser Gly Ser Leu Ser Val Glu Glu Phe Met Ser Xaa Pro Glu

35 40 45

Leu Gln Gln Asn Xaa Leu Val Gln Arg Val Ile Asp Ile Phe Asp Thr

50 55 60

Asp Gly Asn Gly Glu Val Asp Phe Lys Glu Phe Ile Glu Xaa Val Ser

65 70 75 80

Gln Phe Ser Val Lys Gly Asp Lys Glu Gln Lys Leu Arg Phe Ala Phe

85 90 95

Arg Ile Tyr Asp Met Asp Lys Asp Gly Tyr Ile Ser Asn Gly Glu Leu

100 105 110

Phe Gln Xaa Xaa Lys Met Met Val Gly Asn Asn Leu Lys Asp Thr Gln

115 120 125

Leu Gln Gln Ile Val Asp Lys Thr Ile Ile Asn Ala Asp Lys Asp Xaa

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Asp Ile His Lys Lys Met Val Val Asp Val

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Arg Gly Ser His His His His His His Gly Ser Met Ser Gly Arg Arg
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Phe His Leu Ser Thr Thr Asp Arg Val Ile Lys Ala Val Pro Phe Pro
20 25 30

cca acc caa cgg ctt act ttc aag gaa gta ttt gag aat ggg aaa cct 261
Pro Thr Gln Arg Leu Thr Phe Lys Glu Val Phe Glu Asn Gly Lys Pro
35 40 45

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Lys Val Asp Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu Glu
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 Glu Glu Val Ala Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu Arg
 70 75 80

caa gag aag act atg ata gaa gta gat gct cca atc aca gta tgt ggt 405
 Gln Glu Lys Thr Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys Gly
 85 90 95

gat att cat gga caa ttc ttt gac cta atg aag tta ttt gaa gtt gga 453
 Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly
 100 105 110

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 Gly Ser Pro Ser Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp
 115 120 125

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 Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu Lys
 130 135 140 145

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 165 170 175

tat tcg gaa cag gtg tat gat gcc tgt atg gag aca ttt gac tgt ctt 693
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 180 185 190

cct ctt gct gcc ctc tta aac cag cag ttt ctc tgt gta cat gga gga 741
 Pro Leu Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly
 195 200 205

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 Met Ser Pro Glu Ile Thr Ser Leu Asp Asp Ile Arg Lys Leu Asp Arg
 210 215 220 225

ttt acg gaa cct ccc gcc ttt gga cct gtg tgt gac ctg ctt tgg tct 837
 Phe Thr Glu Pro Pro Ala Phe Gly Pro Val Cys Asp Leu Leu Trp Ser
 230 235 240

gat ccc tca gag gat tat ggc aat gag aag acc ttg gag cac tat acc 885
 Asp Pro Ser Glu Asp Tyr Gly Asn Glu Lys Thr Leu Glu His Tyr Thr
 245 250 255

cac aac act gtc cga ggg tgc tct tat ttc tac agt tac cct gca gtt 933
 His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala Val
 260 265 270

tgt gaa ttt ttg cag aac aat aat tta cta tca att atc aga gcc cat 981
 Cys Glu Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His
 275 280 285

gaa gcc caa gat gct ggg tat cga atg tac agg aag agc caa gcc aca 1029
 Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Ala Thr
 290 295 300 305

ggc ttt cca tca ctt att aca att ttc tct gcc ccc aat tac cta gat 1077
 Gly Phe Pro Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu Asp
 310 315 320

gtc tat aac aat aaa gct gct gtg ttg aaa tat gaa aac aat gtc atg 1125
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 325 330 335

aat atc agg cag ttt aac tgt tct cca cac ccc tac tgg ctt cca aac 1173
 Asn Ile Arg Gln Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro Asn
 340 345 350

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 355 360 365

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 Thr Glu Met Leu Val Asn Val Leu Asn Ile Cys Ser Asp Asp Glu Leu
 370 375 380 385

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ccc aca ggc aca ctc cct ctg ggc gtc ctc tca gga ggc aag cag act 1461
Pro Thr Gly Thr Leu Pro Leu Gly Val Leu Ser Gly Gly Lys Gln Thr
435 440 445

atc gag aca gcc atc aga ggg ttc tgg ctt cag cac aag atc cgg agt 1509
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cga aag gat agc ata tac cct ggt ggg cca atg aaa tct gta acc tca 1605
Arg Lys Asp Ser Ile Tyr Pro Gly Gly Pro Met Lys Ser Val Thr Ser
485 490 495

gca cac tca cat gct gcg cac agg agc gac caa ggg aag aaa gcc cat 1653
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Ser Met Gly
515

aat gag gca agt tat cct ttg gaa atg tgc tca cac ttt gat gca gat 1755
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gtg cta aag atg atg gtg ggg aac aat ctg aaa gat aca cag tta cag 2091
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aga ata tcc ttt gaa gaa ttc tgt gct gtt gta ggc ggc cta gat atc 2187
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cac aaa aag atg gtg gta gat gtg tga ttaattagaa gcttaattag 2234
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 680 685

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35 40 45

Pro Lys Val Asp Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu
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Glu Glu Glu Val Ala Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu
65 70 75 80

Arg Gln Glu Lys Thr Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys
85 90 95

Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val
100 105 110

Gly Gly Ser Pro Ser Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val
115 120 125

Asp Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu
130 135 140

Lys Ile Asn His Pro Lys Thr Leu Phe Leu Leu Arg Gly Asn His Glu
145 150 155 160

Cys Arg His Leu Thr Asp Tyr Phe Thr Phe Lys Gln Glu Cys Arg Ile
165 170 175

Lys Tyr Ser Glu Gln Val Tyr Asp Ala Cys Met Glu Thr Phe Asp Cys
180 185 190

Leu Pro Leu Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly
195 200 205

Gly Met Ser Pro Glu Ile Thr Ser Leu Asp Asp Ile Arg Lys Leu Asp
210 215 220

Arg Phe Thr Glu Pro Pro Ala Phe Gly Pro Val Cys Asp Leu Leu Trp
225 230 235 240

Ser Asp Pro Ser Glu Asp Tyr Gly Asn Glu Lys Thr Leu Glu His Tyr
245 250 255

Thr His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala
260 265 270

Val Cys Glu Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala
275 280 285

His Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Ala
290 295 300

Thr Gly Phe Pro Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu
305 310 315 320

Asp Val Tyr Asn Asn Lys Ala Ala Val Leu Lys Tyr Glu Asn Asn Val
325 330 335

Met Asn Ile Arg Gln Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro
340 345 350

Asn Phe Met Asp Val Phe Thr Trp Ser Leu Pro Phe Val Gly Glu Lys
355 360 365

Val Thr Glu Met Leu Val Asn Val Leu Asn Ile Cys Ser Asp Asp Glu
370 375 380

Leu Ile Ser Asp Asp Glu Ala Glu Gly Ser Thr Thr Val Arg Lys Glu

385 390 395 400
 Ile Ile Arg Asn Lys Ile Arg Ala Ile Gly Lys Met Ala Arg Val Phe
 405 410 415
 Ser Ile Leu Arg Gln Glu Ser Glu Ser Val Leu Thr Leu Lys Gly Leu
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 Thr Pro Thr Gly Thr Leu Pro Leu Gly Val Leu Ser Gly Gly Lys Gln
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 Thr Ile Glu Thr Ala Ile Arg Gly Phe Ser Leu Gln His Lys Ile Arg
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 Ser Phe Glu Glu Ala Arg Gly Leu Asp Arg Ile Asn Glu Arg Met Pro
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His Ser

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 35 40 45
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 50 55 60

Asp Gly Asn Gly Glu Val Asp Phe Lys Glu Phe Ile Glu Gly Val Ser
65 70 75 80

Gln Phe Ser Val Lys Gly Asp Lys Glu Gln Lys Leu Arg Phe Ala Phe
85 90 95

Arg Ile Tyr Asp Met Asp Lys Asp Gly Tyr Ile Ser Asn Gly Glu Leu
100 105 110

Phe Gln Val Leu Lys Met Met Val Gly Asn Asn Leu Lys Asp Thr Gln
115 120 125

Leu Gln Gln Ile Val Asp Lys Thr Ile Ile Asn Ala Asp Lys Asp Gly
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Asp Gly Arg Ile Ser Phe Glu Glu Phe Cys Ala Val Val Gly Gly Leu
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Asp Ile His Lys Lys Met Val Val Asp Val
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CGGTAGAGGC CCGGGAAGCC, interaction domain with
cytoskeleton, death-domain homolog, stomatin
homolog

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Met

1

aga gga tgc cat cac cat cac cat cac gga tcc atg tcc ggg agg cgc 165

Arg Gly Ser His His His His His His Gly Ser Met Ser Gly Arg Arg

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ttc cac ctc tcc acc acc gac cgc gtc atc aaa gct gtc ccc ttt cct 213

Phe His Leu Ser Thr Thr Asp Arg Val Ile Lys Ala Val Pro Phe Pro

20 25 30

cca acc caa cgg ctt act ttc aag gaa gta ttt gag aat ggg aaa cct 261

Pro Thr Gln Arg Leu Thr Phe Lys Glu Val Phe Glu Asn Gly Lys Pro

35 40 45

aaa gtt gat gtt tta aaa aac cat ttg gta aag gaa gga cga ctg gaa 309

Lys Val Asp Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu Glu

50 55 60 65

gag gaa gta gcc tta aag ata atc aat gat ggg gct gcc atc ctg agg 357

Glu Glu Val Ala Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu Arg

70 75 80

caa gag aag act atg ata gaa gta gat gct cca atc aca gta tgt ggt 405

Gln Glu Lys Thr Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys Gly

85 90 95

gat att cat gga caa ttc ttt gac cta atg aag tta ttt gaa gtt gga 453

Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val Gly

100 105 110

gga tca cct agt aac aca cgc tac ctc ttt ctg ggt gac tat gtg gac 501
 Gly Ser Pro Ser Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val Asp
 115 120 125

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 Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu Lys
 130 135 140 145

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 Ile Asn His Pro Lys Thr Leu Phe Leu Leu Arg Gly Asn His Glu Cys
 150 155 160

agg cat ctt aca gac tat ttc acc ttc aaa cag gaa tgt cga atc aaa 645
 Arg His Leu Thr Asp Tyr Phe Thr Phe Lys Gln Glu Cys Arg Ile Lys
 165 170 175

tat tcg gaa cag gtg tat gat gcc tgt atg gag aca ttt gac tgt ctt 693
 Tyr Ser Glu Gln Val Tyr Asp Ala Cys Met Glu Thr Phe Asp Cys Leu
 180 185 190

cct ctt gct gcc ctc tta aac cag cag ttt ctc tgt gta cat gga gga 741
 Pro Leu Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly Gly
 195 200 205

atg tca cct gaa att act tct tta gat gac att agg aaa tta gac agg 789
 Met Ser Pro Glu Ile Thr Ser Ser Leu Asp Asp Ile Arg Lys Leu Asp Arg
 210 215 220 225

ttt acg gaa cct ccc gcc ttt gga cct gtg tgt gac ctg ctt tgg tct 837
 Phe Thr Glu Pro Pro Ala Phe Gly Pro Val Cys Asp Leu Leu Trp Ser
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gat ccc tca gag gat tat ggc aat gag aag acc ttg gag cac tat acc 885
 Asp Pro Ser Glu Asp Tyr Gly Asn Glu Lys Thr Leu Glu His Tyr Thr
 245 250 255

cac aac act gtc cga ggg tgc tct tat ttc tac agt tac cct gca gtt 933
 His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala Val
 260 265 270

tgt gaa ttt ttg cag aac aat aat tta cta tca att atc aga gcc cat 981
 Cys Glu Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala His
 275 280 285

gaa gcc caa gat gct ggg tat cga atg tac agg aag agc caa gcc aca 1029
 Glu Ala Gln Asp Ala Gly Tyr Arg Met Tyr Arg Lys Ser Gln Ala Thr
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gtc tat aac aat aaa gct gct gtg ttg aaa tat gaa aac aat gtc atg 1125
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 325 330 335

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 Asn Ile Arg Gln Phe Asn Cys Ser Pro His Pro Tyr Trp Leu Pro Asn
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 Thr Glu Met Leu Val Asn Val Leu Asn Ile Cys Ser Asp Asp Glu Leu
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 Gly Phe Ser Leu Gln His Lys Ile Arg Ser Phe Glu Glu Ala Arg Gly
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ctg gac cga att aat gag cga atg cca ccc cga aag gat agc ata tac 1605
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cct ggt ggg cca atg aaa tct gta acc tca gca cac tca cat gct gcg 1653
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cag cga gta ata gat ata ttc gac aca gat ggg aat gga gaa gta gac 1944
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gac ggc tat att tcc aat ggg gaa ctc ttc cag gtg cta aag atg atg 2088
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Pro Lys Val Asp Val Leu Lys Asn His Leu Val Lys Glu Gly Arg Leu
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Glu Glu Glu Val Ala Leu Lys Ile Ile Asn Asp Gly Ala Ala Ile Leu
65 70 75 80

Arg Gln Glu Lys Thr Met Ile Glu Val Asp Ala Pro Ile Thr Val Cys
85 90 95

Gly Asp Ile His Gly Gln Phe Phe Asp Leu Met Lys Leu Phe Glu Val
100 105 110

Gly Gly Ser Pro Ser Asn Thr Arg Tyr Leu Phe Leu Gly Asp Tyr Val
115 120 125

Asp Arg Gly Tyr Phe Ser Ile Glu Cys Val Leu Tyr Leu Trp Ser Leu
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Lys Ile Asn His Pro Lys Thr Leu Phe Leu Leu Arg Gly Asn His Glu
145 150 155 160

Cys Arg His Leu Thr Asp Tyr Phe Thr Phe Lys Gln Glu Cys Arg Ile
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Lys Tyr Ser Glu Gln Val Tyr Asp Ala Cys Met Glu Thr Phe Asp Cys
180 185 190

Leu Pro Leu Ala Ala Leu Leu Asn Gln Gln Phe Leu Cys Val His Gly

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 Gly Met Ser Pro Glu Ile Thr Ser Leu Asp Asp Ile Arg Lys Leu Asp
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 225 230 235 240
 Ser Asp Pro Ser Glu Asp Tyr Gly Asn Glu Lys Thr Leu Glu His Tyr
 245 250 255
 Thr His Asn Thr Val Arg Gly Cys Ser Tyr Phe Tyr Ser Tyr Pro Ala
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 Val Cys Glu Phe Leu Gln Asn Asn Asn Leu Leu Ser Ile Ile Arg Ala
 275 280 285
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 Thr Gly Phe Pro Ser Leu Ile Thr Ile Phe Ser Ala Pro Asn Tyr Leu
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